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Dr. J. Lederberg Box 115 1230 York Avenue New York, NY 10021

Dear Joshua:

I've attached a rough comparison of current and proposed chemical routes to methyl methacrylate and compared these to a speculative biological route based on isobutane. As you would anticipate a high yield biological isobutane route offers a significant advantage in (1990) raw material costs. There are obviously a number of various routes from isobutane to methyl methacrylate, but I recently came across an interesting paper in J. Chem Soc. Perkin I p. 1404 (1979) that discusses the conversion of isobutyric acid to the β -hydroxy derivative via a proposed methacrylate intermediate. We're following up on this because of the interest in the selectivity of the hydroxylation (β vs. α) and the proposed dehydrogenation of the acid.

As to 2-methyl-lactic acid, there are references to its polymerization to form poly(α -hydroxyisobutyric acid) which should be a biodegradable material (compare to polylactic, polyglycolic and poly β -hydroxybutric - the former are of interest as absorbable sutures and controlled release materials and the latter is the storage material ICI is currently pushing).

I agree that the metabolism of isobutane (and isobutane) is very worthwhile due to the anticipated low cost of this hydrocarbon. We will shortly be isolating organisms which grown on isobutane. In addition, a methyl lactate polymer (or copolymer) might have some interesting specialty uses (dependant of course on its properties) and this would be a bonus from isobutane metabolism research.

Very truly yours

Sol J. Barer

Manager, Biotechnology

SJB:mg

P.S. Sorry for the delay in writing to you. I did not receive your letter directly - only by copy from Don Wilson!

cc: L. I. Peterson

I. SUMMARY

The various chemical processes (commercial and non-commercial) for the production of methyl methacrylate are described below followed by our most recent economic analyses of such processes. These chemical routes are then compared with speculative biological processes (based on isobutane oxidation) in terms of 1990 raw material costs (as a first order approximation, I am assuming equal capital costs). The results indicate that the biological processes could be significantly better than the present or proposed chemical processes (1990 raw material costs ~1/3 lower than the best projected chemical technology). This is due, of course, to the potential high yield obtainable via the highly selective nature of the biotransformation.

II. CHEMICAL ROUTES

A. Acetone Processes

The current commercial process practiced by Rohm & Haas involves the conversion of acetone into acetone cyanohydrin, followed by hydrolysis and esterification to MMA.

$$H_3^{C} C = O + HCN \xrightarrow{OH^-} H_3^{C} C \xrightarrow{CN} \frac{1) \triangle/H_2SO_4}{2) \text{ MeOH}} \xrightarrow{CH_2} C-CO_2Me$$

B. Isobutylene

Different routes from isobutylene to MMA have been developed but low selectivity hinders commercialization. These routes involve the oxidation of isobutylene to α -methyl-lactic acid followed by dehydration or the oxidation of isobutylene via methacrolein to methacrylic acid.

C. Propylene Route

Propylene is converted to isobutyraldehyde followed by oxidation to isobutyric acid which is then dehydrogenated (as the acid or ester) to the unsaturated product. In the MIB (methyl isobutyrate) process esterification precedes dehydrogenation.

D. Isobutane Route

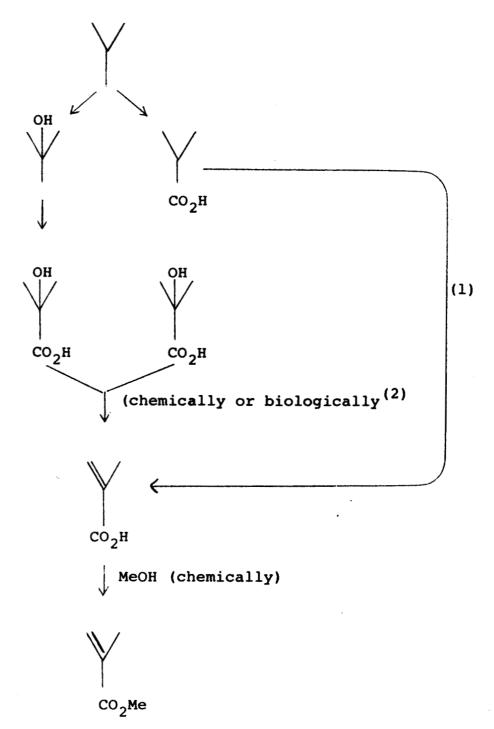
This is a speculative route involving the oxidation of isobutane to isobutyric acid followed by dehydrogenation and esterification to yield MMA.

III. CURSORY ECONOMICS FOR CHEMICAL ROUTES TO METHYL METHACRYLATE

	<u>Status</u>		Economics	
Process		Raw Material Efficiency, %	Basis	IUTV 1990 ¢/1b.
Acetone Cyanohydrin	Commercial	Acetone - 85	Reinvestment Pricing	137
		HCN - 84	Zero Cash Flow Acetone and HCN	125
		MeOH - 87	Gas Pool Value Acetone and Fuel Value HCN	87
MIB (Isobutyraldehyde	New	Propylene - 69	Reinvestment	91
Oxidation) - Chem Systems		CO - 69		
		MeOH - 73		
Isobutylene Oxidation - SRI/Celanese	New	Isobutylene - 72	Reinvestment	100
		Methanol - 97		
Isobutyric Acid Dehydrogenation		Isobutyric Acid- 98	Reinvestment	93
20 a. 0 30 u		Methanol - 98	t.	
Isobutane Oxidation	Speculative	Isobutane - 56	Reinvestment	94
		Methanol - 97		

IV. BIOLOGICAL ROUTES TO MMA

The key in any biological process of this sort would be the ability to selectively functionalize isobutane in high yield. If such a high yield biotransformation could be achieved, a very competitive biological route to MMA could be developed as evidenced by the raw material costs (1990) of the various competitive routes. A number of options in the development of such a process could be envisioned (as diagrammed below):



- (1) Work at MIT with C. Propionicum.
- (2) Via a dehydrating enzyme.

V. APPROXIMATE 1990 RAW MATERIAL COSTS OF VARIOUS MMA PROCESSES

Chemical Process	Raw Material Yield	~ Cost ¢/lb. MMA	~ Total Cost ¢/lb. MMA
Cyanohydrin Route	Acetone - 85%	30	
	HCN - 84%	29	69 ,
	MeOH - 87%	10	
	_		
MIB	C ₃ - 69%	32	
	CO - 69%	12	46
	MeOH - 73%	12	
	_		
Isobutylene Oxidation	C ₄ = - 72%	31	40
	MeOH - 97%	9	
Isobutane	C ₄ - 56%	31	40
	•		
	MeOH - 97%	9	
Biological Process			
Isobutane	C ₄ - 95%	18	27
	MeOH - 97%	9	